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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/982,223	10/18/2001	George Q. Daley	13086-002001	7405

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,223	DALEY ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,24-26,34-36 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,24-26,34-36 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 13, 2005 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 depends from itself, and claim 34 depends from claim 26. Because the claim is dependent on itself, it is unclear what limitations are and are not a part of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman (as recited in the previous Office Action) in view of Lin (US 5,861,155; see entire document).

Kingsman teaches a retroviral vector comprising a 5' LTR, a portion of the HIV1 *gag* packaging sequence gene (specifically nucleotides 791-1143 of the full length sequence, which corresponds to the amino-terminal region of HIV *gag*) altered at its three ATG codons (including the *gag* initiator codon), a multicloning site (comprising a number of restriction sites for the insertion of a heterologous gene), and a 3' LTR (i.e., a proviral recovery sequence) (see for example Figure 3, in combination with column 7, lines 53-58, and column 9, line 43). Importantly, Kinsman teaches that the 3' LTR region used in their vector has been designed to contain several convenient restriction sites in order to allow the easy replacement/swapping of different promoter elements into the LTR (see for example column 7, lines 23-26). Kingsman also teaches using the amino terminal portion of the *gag* sequence, wherein the amino terminal portion of the *gag* sequence is altered in at least two codons. Additionally, Kingsman teaches the alteration of all three of the nucleotides of the initiation codon (ATG->TAA; see SEQ ID NO: 1, residues 21-23, at column 8, lines 15-16). Finally, Kingsman teaches that a heterologous insert sequence can be cloned into the vector (see for example column 4, lines 18-40) for gene therapy or marker expression purposes.

As it regards claim 6, it is noted that "a portion of the nucleotide sequence of SEQ ID NO: 2" is any nucleic acid, such as adenine; the vector taught by Kingsman comprises adenine, and therefore Kingsman meets the limitation of claim 6.

As it regards claims 8-10, it is important to note that there is no specific sequence requirement for the claim; i.e., the claim does not require that the packaging sequence is SEQ ID

NO: 1 having an altered codon sequence at positions 1097-1099 and/or 1589-1591. Rather, the limitation only requires that a sequence corresponding to 1097-1099 and/or 1589-1591 be altered from an ATG. Effectively, this can be interpreted as *any* sequence that lines up to 1097-1099 and/or 1589-1591 of SEQ ID NO: 1, and wherein the corresponding sequence in each position is not ATG, because the relationship in lining up the sequences is arbitrary within the limitations of the claim. Because the HIV *gag* sequence taught by Kingsman can line up with SEQ ID NO: 1 in various embodiments where the corresponding positions at 1097-1099 and/or 1589-1591 are not ATG, this limitation is also taught by Kingsman.

Although Kingsman meets all of the limitations set forth above, Kingsman does not specifically teach the use of *Not*I, *Sfi*I, *Pac*I or P1-*Sce*I as the restriction sites in the 3'LTR region.

Lin teaches that polylinkers containing restriction sites such as *Sfi*I or *Not*I are convenient for cloning purposes (see for example column 27, lines 34-41).

It would be obvious for the ordinary skilled artisan to use *Not*I, *Sfi*I, *Pac*I or P1-*Sce*I as the restriction sites in the 3'LTR region of the vector taught by Kingsman because Kingsman specifically says that engineering the 3'LTR region of their vector to contain restriction sites useful for cloning of alternative promoters is desirable, and Lin specifically indicates that restriction sites such as *Not*I or *Sfi*I are useful for cloning purposes. The ordinary skilled artisan would have been motivated to combine the teachings of Kingsman and Lin in order to use any convenient or useful restriction site for the purpose of cloning, as suggested by Kingsman, and for which Lin teaches the aforementioned sites are convenient and useful. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success

when substituting any of *Not*I, *Sfi*I, *Pac*I or P1-*Sce*I as the restriction sites in the 3'LTR region of the vector taught by Kingsman.

Claims 1-12 and 24*, 25*, 34-36* and 47* are rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman and Lin (as applied to claims 1-12 above), and further in view of Beach et al. (US 6,025,192; see entire document; henceforth Beach). Note- "*" represents the claims that are specifically rejected by the combination of references.

Kingsman and Lin disclose the limitations as set forth above in the rejection of claims 1-12 under 35 USC § 103(a). Briefly, the teach a vector comprising a packaging sequence, a cloning site, and a 3' LTR comprising restriction sites selected from the group consisting of *Not*I, *Sfi*I, *Pac*I and P1-*Sce*I, wherein at least two codons of the packaging sequence are altered so as to reduce the formation of fusion polypeptides.

However, Kingsman and Lin do not specifically disclose the inclusion of a bacterial origin of replication and bacterial selection marker (i.e., replicon) in their vector, nor do they teach the inclusion of a recombinase site in the 3' LTR of their vector.

Beach teaches a viral vector construct comprising a 3' LTR sequence comprising a proviral excision element (i.e., a proviral recovery sequence), a packaging signal and a bacterial replicon comprising an origin of replication and a selection marker (see for example column 3, lines 33-46). Beach also teaches that any bacterial selection marker can be used (see for example column 5, lines 1-18), such as a bleomycin marker sequence. In a specific embodiment, the proviral excision element is a recombinase signal such as loxP, along with a rare restriction enzyme such as *Not*I (see for example column 4, lines 32-40). Finally, Beach teaches that

presence of the loxP and rare restriction cutter site are useful for excising genes (i.e., the loxP recombinase site is a useful proviral recovery sequence) from a recipient cell (see for example column 4, lines 10-51).

It would have been obvious for the skilled artisan to combine these teachings to construct a vector with a bacterial replicon and a 3'LTR containing a recombinase site because the recombinase serves as a proviral recovery sequence, and Kingsman and Lin clearly indicate that their vector should contain a proviral recovery sequence (see for example Figure 3, in combination with column 7, lines 53-58, and column 9, line 43); thus, the use of a recombinase (as taught by Beach) is merely a species of the genus of proviral recovery sequences to be used in the vector taught by Kingsman and Lin. The ordinary skilled artisan would have been motivated to combine the teachings of Kingsman and Lin with the teachings of Beach in order to use a proviral recovery sequence that has a well-characterized mechanism (such as loxP – mediated recombination) as well as to use a create a vector that contains a bacterial replicon, and thus can be produced in large quantities by using bacteria. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when combining the teachings of Kingsman and Lin with the teachings of Beach.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Au 1636

JAMES KETTER
PRIMARY EXAMINER